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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/821,832	03/30/2001	Thomas Tuschl	0399.2008-002	6240

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EXAMINER
CHUNDURU, SURYAPRABHA

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 01/23/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/821,832	Applicant(s) TUSCHL ET AL.	
	Examiner Suryaprabha Chunduru	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-75* is/are pending in the application.

4a) Of the above claim(s) *6-11,13-15 and 17-71* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,12,16 and 72-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The response to restriction requirement (Paper No. 17) filed on December 6, 2002 has been entered and considered.

2. The Information Disclosure Statement (Paper Nos. 14 and 18) filed on June 10, 2002 and December 6, 2002 the Preliminary Amendment (Paper No. 10) filed on February 26, 2002 have been entered and considered.

3. Applicant's election with traverse of Group I (claims 1-5, 12, 43, 48-50, 72-75) in Paper No. 17 is acknowledged. The traversal is on the ground(s) that the subject matter of the claims in Group I and III-X substantially overlaps and would not be a serious burden on the examiner. This is found not persuasive because claims in Groups III-X are drawn to different methods and products which are classified in separate class and subclass as compared to the product claims in Groups I. Applicants' argument regarding undue burden, is fully considered but found not persuasive because classification is prime basis for restriction which has not been rebutted simply because of the overlapping subject matter occurring in some cases does not eliminate the burden in this case. Each case is examined on its own merits further (i) the issues are not the same with respect to 35 U.S.C.112 and 35 U.S.C. 101 statutes, (ii) separate Art Units would examine the different Groups under ordinary circumstances. Thus the restriction requirement is still deemed proper.

4. Claims in Group I are considered for examination in this office action. Claim 43 is withdrawn from further consideration because it belongs to the Group II. Claim 16 is considered for examination as it belongs to Group I but by error classified in Group III. Hence claims 1-5,

12, 16, 48-50, 72-75 are considered for examination in this office action. Claims 6-11, 13-15, 17-47, 51-71 are withdrawn from further consideration.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 12, 16, 48-50, 72-75 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The current claims are drawn to an isolated RNA or DNA encoding said RNA of from about 21 to about 23 nucleotides that mediates RNA interference of an mRNA to which it corresponds, and are also drawn to an analog or variants of an isolated RNA which vary by addition, deletion, substitution or alteration of one or more nucleotides. This large genus of variants is represented in the specification by the modified analog. Thus, applicants have expressed possession of only one species in a genus, which comprises hundreds of millions of different possibilities. The written description guidelines note regarding such genus/species situations that "Satisfactory disclosure of a ``representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.) Here, no common elements or attributes of the

structural information (sequences) are disclosed. With regard to the isolated RNA, it is insufficient to demonstrate identity of regulatory activity (mediates RNA interference) where no structural information regarding where in the RNA the activity resides. Further no information is given regarding a methodology to determine such common elements or attributes. Further, there is no description of variants.

With regard to the written description, all of the claims drawn to an RNA or an analog of isolated RNA, or an isolated DNA encoding said RNA, encompass different structural limitations, for which, no structural limitation is provided in the specification. It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, only the amino acid sequence of the disclosed SEQ ID No. 2 is described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that: "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In this application at the time of filing, there is no record or description, which would demonstrate conception or written description of any structural information of isolated RNA or an analog of an isolated RNA or isolated DNA encoding said RNA with retaining correlative function in the claimed product.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 12, 16, 48-50 are rejected under 35 U.S.C. 102(b) as being anticipated by Zamore et al. (Biochemistry, Vol. 38, pp. 596-604, 1999).

With reference to claims 1, 12, 16, Zamore et al teach translational regulation of hunchback mRNA, wherein Zimore et al. teach an isolated RNA of from about 21 to 23 nucleotides that mediates RNA interference of an mRNA to which it corresponds (see page 598, column 1, paragraph 4, page 599, column 2, Fig 2A, page 600, column 2, lines 6-12).

With reference to the instant claims 2-5, Zamore et al. also teach that (i) shorter RNA having 22 nucleotides abolished (inactivates) the RNA binding activity (transcriptional activity) (see page 600, column 2, lines 6-12) and RNA comprises 3' UTR (see page 599, column 2, paragraph 1) (ii) chemical synthesis of RNA or analog of a naturally occurring RNA (see page 598, column 1, paragraph 4); (iii) analogs differs by addition of 5'-guanosines (see page 599, column 2, Fig 2A).

With reference to claims 48-50, Zamore et al. teach RNA isolation by non-denaturing gel electrophoresis and column chromatography (see page 598, column 1, paragraphs 1-3, column 2, paragraph 1).

Thus the disclosure of Zamore et al. meets the limitations in the instant claims.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 72-75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zamore et al. (Biochemistry, Vol. 38, pp. 596-604, 1999) in view of Wassenegger et al. (USPN. 6,218,142).

With reference to claims 72-75, Zamore et al teach translational regulation of hunchback mRNA, wherein Zamore et al. teach an isolated RNA of from about 21 to 23 nucleotides that mediates RNA interference of an mRNA to which it corresponds (see page 598, column 1, paragraph 4, page 599, column 2, Fig 2A, page 600, column 2, lines 6-12). How ever, Zamore et al. did not teach a DNA encoding said RNA processed in eukaryotic cells (expression vector).

Wassenegger et al. teach nucleic acid molecules encoding coding region (mRNA) of RNA-directed RNA polymerase or encoding an enzymatically active fragment (see column 45, lines 18-40). Wassenegger et al. also teach transcriptional expression of said nucleic acid

molecule in eukaryotic cells (see column 5, lines 66-67, column 6, lines 1-14, column 45, lines 54-57, column 46, lines 17-18).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to combine the transcriptional regulator RNA as taught by Zamore et al. with the expression system as taught by Wassenegger et al. to achieve expected advantage of developing an efficient expression vector because Wassenegger et al. suggests that "whenever a transgene expression comes up to a threshold dose it is without selective pressure silenced either by transcriptional or post transcriptional inactivation. Common to this model is the assumption that antisense RNAs are synthesized from sense RNA templates by an RNA-directed RNA polymerase (RdRP). To provide a detailed examination of RNA-mediated gene regulation, novel nucleic acid molecules encoding RdRP are linked to regulatory elements allowing expression in prokaryotic/ eukaryotic host cells (see column 1, lines 7-67, column 2, lines 1-35). An ordinary practitioner would have been motivated to combine the teachings of Zamore et al. with the expression system of Wassenegger et al. to achieve wide use of the isolated RNA molecules by incorporating the expression system because these limitations would improve the characterization of the nucleic acids.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 703-305-1004. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's

supervisor, Gary Benzion can be reached on 703-305-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
January 21, 2003

JEFFREY FREDMAN
PRIMARY EXAMINER